

PREFACE

Current Advanced Statistical Issues in Clinical Research—Adaptive Designs and Translational Medicine

Recently, with the availability of genomic technologies and other new science, the biotechnology and pharmaceutical industries have attracted much global attention. However pharmaceutical development is a risky, complex, costly, and time-consuming endeavor. It usually takes more than 12 years with an average cost between 800 million and one billion US dollars to develop a drug from screening of candidates to regulatory approval for commercial marketing. A hefty 70% of the cost for pharmaceutical development is wasted on drugs that do not even make it to market. In addition, more than half of the development duration is spent in clinical trials. Despite better understanding of disease etiology, a rapid increase in resources, technological advances, seemingly great number of potential candidates and a longer development duration, the performance of drug development is disappointing. In fact, only one out of 10,000 candidates screened in the laboratory will survive to the market launch. More than 60% of the potential candidates that enter into clinical development fail. Furthermore, the success rate of the phase III stage of clinical development has fallen by 30%. As a result, the total duration of drug development is increased.

The latest advanced high-throughput technology is generating a far greater number of potential drug candidates than before to reach clinical development. But the success rate of drug registration has declined drastically in recent years. One of the many possible reasons for the unsatisfactory performance is that the current paradigm for drug development is no longer functioning for the 21st century. Therefore, new concepts, strategies, and methodology are urgently needed to reduce the development cost, to shorten the development duration, and to improve the development success rate. In recent years, the use of adaptive

design methods in clinical research and development based on accrued data has become very popular due to its flexibility and efficiency. In clinical trials, it is not uncommon to modify trial and/or statistical procedures during the conduct of clinical trials based on the review of interim data. The purpose is not only to efficiently identify the clinical benefits of the test treatment under investigation and save time and money, but also to increase the probability of success of clinical development. As a result, adaptive designs seem to open a whole new territory for drug development and represent an opportunity to gain dramatic efficiencies during the drug development process.

In recent years, how to apply basic research discoveries to the development of trials and studies in humans has attracted much attention. Such basic research is typically conducted in the laboratory, or in preclinical studies in which scientists study disease at a molecular or cellular level. Translational medicine refers to the translation of basic scientific discoveries into practical applications. More specifically, translational research moves basic discoveries from the laboratory (“the bench”) into clinical practice to diagnose and treat patients (“bedside”). Under this new approach, basic scientists can offer clinicians new tools for use in patients, and clinicians can gain more insight about the nature and progression of disease to motivate basic research. Translational medicine incorporates aspects of both basic science and clinical research, and consequently forms a powerful practice that accelerates clinical research.

Both adaptive designs and translational medicine research play important roles in a scientific manner to pharmaceutical research. However, the statistical work to draw a statistical inference with regard to translational medicine research is

still in a preliminary stage. On the other hand, although there are many adaptive design methods available, how adaptive design can be optimized remains a critical issue.

To aid comprehensive understanding of the statistical designs and methodology that are commonly employed in adaptive designs and translational research, and with the support of the Bureau of Pharmaceutical Affairs, Department of Health, Taiwan, the National Health Research Institutes and Formosa Cancer Foundation organized two symposiums on “Current Advanced Statistical Issues in Clinical Trials—Adaptive Designs”, held on November 25, 2006, and “Current Advances in Evaluation of Research and Development of Translational Medicine”, held

on October 19, 2007, in Taipei, Taiwan. Both symposiums attracted more than 400 participants and received important research attention in Taiwan. In celebration of this success, this special issue of the *Journal of the Formosan Medical Association*, “Current Advanced Statistical Issues in Clinical Research—Adaptive Designs and Translational Medicine” includes 10 works that were presented at the two symposiums. Through this special issue, we hope that readers will more fully understand the statistical issues surrounding adaptive designs and translational medicine.

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